of bands because other cells may be more important in forming the antibody proteins.

In this connection differences in the protein of γG-antibody formed for two different haptens by a single rabbit have been reported (*14*). Also, Sela and Mozes (*15*) showed that the nature of the carrier protein of the antigen affects the protein type of γG-antibody formed against a single hapten. The differences could be due to the production of antibody by different cells.

The differences in gel patterns of H-chains from antibody of the same specificity but from different rabbits could be due to a variation in the relative distribution of these different antibody-producing cell types in individual rabbits.

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**References and Notes**

1. Nomenclature according to *Bull. World Health Organ.* **30**, 447 (1964).
2. J. Rejnek, J. Kostka, O. Kotynek, *Nature* **209**, 926 (1966).
3. B. J. Davis, *Ann. N.Y. Acad. Sci.* **121**, 404 (1964).
4. O. Roholt, G. Radzimski, D. Pressman, *J. Exp. Med.* **122**, 785 (1965).
5. ———, *Science* **147**, 613 (1965).
6. R. A. Reisfeld, U. J. Lewis, D. E. Williams, *Nature* **195**, 281 (1962); *Chemical Formulation for Disc Electrophoresis*, (Canal Industrial Corporation, Bethesda, Maryland, April, 1965).
7. O. Roholt and D. Pressman, in preparation.
8. C. Tanford, *Physical Chemistry of Macromolecules* (Wiley, New York, 1961).
9. Since the electrophoresis was at *p*H 4.3, an additional carboxyl group would add only a fractional charge and an amino group a whole charge.
10. R. A. Reisfeld, S. Dray, A. Nisonoff, *Immunochemistry* **2**, 155 (1965).
11. S. Cohen and R. R. Porter, *Biochem. J.* **90**, 278 (1964).
12. S. Utsumi and F. Karush, *Biochemistry* **3**, 1329 (1964).
13. D. Pressman, *Ann. N.Y. Acad. Sci.* **101**, 253 (1962); ———, A. L. Grossberg, O. Roholt, P. Stelos, Y. Yagi, *Ann. N.Y. Acad. Sci.* **103**, 582 (1963).
14. A. L. Grossberg, O. A. Roholt, D. Pressman, *Biochemistry* **2**, 989 (1963); M. Sela, D. Givol, E. Mozes, *Biochim. Biophys. Acta* **78**, 649 (1963).
15. M. Sela and E. Mozes, *NIH Information Exchange 5*, Sci. Memo #75 (1966).
16. Supported in part by NIH grant AI-03962. We thank F. Maenza for technical assistance.

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## Lead-210 and Polonium-210 in Tissues of Cigarette Smokers

Abstract. *Concentrations of lead-210 and polonium-210 in rib bones taken from 13 cigarette smokers were about twice those in six nonsmokers, the polonium-210 being close to radioactive equilibrium with the lead-210. In alveolar lung tissue the concentration of lead-210 in smokers was about twice that in nonsmokers. These differences are attributed to additional intake by inhalation of lead-210.*

Because of the correlation between the smoking of cigarettes and the presence of somatic effects, such as carcinoma of the lung, many studies have been made of the carcinogens present in the smoke. The presence in tobacco of the alpha-emitting and volatile radionuclide $^{210}$Po has lead to several studies correlating the distribution and concentrations of this nuclide in the human body with cigarette smoking. Thus Radford and Hunt (*1*) reported that in the bronchial epithelium of a heavy smoker the activities were such as to produce radiation levels of 165 rem over 25 years. On the other hand, Hill (*2*) and Rajewsky and Stahlhofen (*3*) estimated the doses to be less than 1 and 0.15 rem/year, respectively. Hill (*2*) and Ferri and Baratta (*4*) also showed the $^{210}$Po concentrations in these and other tissues to be higher in smokers than in nonsmokers.

However, because of the relatively short half-life of this nuclide (138 days), its precursor, the lead-210 with a 21.4-year half-life, is also of interest. This nuclide decays by a weak beta-emission to the 5.0-day $^{210}$Bi, which in turn decays by 1.1-Mev beta-emission to $^{210}$Po. The data we present demonstrate that, in skeletal tissues, not only are the concentrations of $^{210}$Po greater in smokers than in nonsmokers, but in both skeletal and lung tissues of smokers the concentrations of $^{210}$Pb are also greater. Moreover, in bone the $^{210}$Po is in radioactive equilibrium with the $^{210}$Pb.

Lead-210 is also shown to be present in the smoke, an association not unexpected since stable lead is known to occur in smoke (*5*) and Nusbaum *et al.* (*6*) have shown correlation between concentrations of lead in bone and cigarette smoking.

Our measurements were made on rib bones and alveolar lung tissue taken at autopsy (or surgery) from subjects of known smoking habits. Individuals smoking more than ten cigarettes daily were classed as smokers, but in our group only one member consumed less than 20.

Activities were determined by wet-ashing the materials in nitric and perchloric acids, converting the solutions to 0.5*N* hydrochloric acid, and plating the $^{210}$Po upon a silver disk. The amount of polonium was determined by counting the disk in a gas-flow internal alpha counter (*7*).

This measurement, along with a replating of the $^{210}$Po grown-in for several months from the $^{210}$Pb in the original solution, and application of the radioactive parent-daughter relation of the Bateman equations, enabled determination of the activity of each of these nuclides at the time of autopsy or surgery. The average errors at the 90-percent confidence level, based on counting statistics, were about 15 percent for $^{210}$Pb and about 20 percent for $^{210}$Po.

Concentrations of $^{210}$Pb and $^{210}$Po in bone are presented in Table 1 along with sexes and ages. The groups are matched by age but not by sex; this mismatch should be examined further, since, as noted earlier (*7, 8*), the skeletal $^{210}$Pb content of women appears to be lower than that of men. Within this particular small group of nonsmokers no statistically significant difference exists.

The mean concentrations of both nuclides in smokers, 0.285 pc $^{210}$Pb and 0.250 pc $^{210}$Po per gram of ash, are more than double those in nonsmokers: 0.135 pc $^{210}$Pb and 0.090 pc $^{210}$Po. Student's *t*-test shows the mean values in the smokers to be significantly higher than in the nonsmokers ($P < .005$).

In smokers the $^{210}$Po is nearly in radioactive equilibrium with its parent ($^{210}$Po : $^{210}$Pb, $0.87 \pm .10$); that the two are closely related is shown by the correlation coefficient of 0.83 ($P < .005$). In nonsmokers a ratio of $0.62 \pm .14$ exists, suggesting a deficiency in content of the daughter; the *t*-test, however, shows the two means to be not quite significantly different ($P < .10$); the correlation coefficient of 0.61 is also low.

The previously reported (*7*) concentration of $^{210}$Pb in trabecular bone (mainly rib and vertebra), $0.184 \pm 0.018$ (S.E.) pc per gram of ash, is significantly lower than that in smokers ($P < .005$) and probably significantly higher than that in nonsmokers ($P < .05$). These differences suggest that the previous sampling of the population was of a mixture of smokers and nonsmokers.

Table 1. Concentrations of $^{210}Pb$ and $^{210}Po$ in rib bones of cigarette smokers and nonsmokers. $^{210}Po$-$^{210}Pb$ correlation coefficients: nonsmokers, 0.61; smokers, 0.83.

| Subject (age, sex) | Concentrations in ash (pc/g) | | $^{210}Po$ : $^{210}Pb$ |
|---|---|---|---|
| | $^{210}Pb$ | $^{210}Po$ | |
| *Nonsmokers* | | | |
| 56, F | 0.071 | 0.021 | 0.30 |
| 57, M | .111 | .030 | .27 |
| 50, M | .117 | .109 | .93 |
| 47, M | .166 | .074 | .45 |
| 76, F | .171 | .180 | 1.05 |
| 61, F | .172 | .124 | 0.72 |
| *Mean ± S.E.* | | | |
| 58 ± 4 | 0.135 ± .016 | 0.090 ± .025 | 0.62 ± .14 |
| *Smokers* | | | |
| 76, M | 0.178 | 0.156 | 0.88 |
| 72, M | .187 | .199 | 1.06 |
| 48, M | .227 | .123 | 0.54 |
| 51, M | .233 | .181 | .78 |
| 60, M | .233 | .138 | .59 |
| 58, M | .252 | .236 | .94 |
| 55, M | .283 | .383 | 1.35 |
| 53, F | .289 | .245 | 0.85 |
| 52, M | .303 | .238 | .78 |
| 53, M | .336 | .275 | .82 |
| 49, M | .341 | .067 | .20 |
| 48, M | .352 | .601 | 1.71 |
| 54, M | .502 | .417 | 0.83 |
| *Mean ± S.E.* | | | |
| 56 ± 2 | 0.285 ± .025 | 0.250 ± .040 | 0.87 ± .10 |

The much-more-limited data from lung tissue appear in Table 2. At 5.9 pc/kg, $^{210}Pb$ in heavy smokers is about 4 times that in nonsmokers. (In these instances $^{210}Po$ was not determined because more than a year elapsed between autopsy and analysis.) It is of interest that subject 22 had a level about twice that of other smokers; this finding may reflect the fact that he had smoked to the day he died, whereas the others, by desisting about a year before death, had enabled some clearance of the $^{210}Pb$.

The correlations between cigarette smoking and the concentrations of nuclides in the lungs and skeletons of these subjects indicate that smoke is a significant source of intake of these nuclides. However, if we assume that our measurements represent the whole body, the known levels of $^{210}Po$ in smoke (*1, 2, 9*) cannot account for the higher skeletal concentrations of this nuclide in smokers. If we assume the validity of the exponential model for nuclide metabolism described in the I.C.R.P. report (*10*), in which retention in the body of the $^{210}Po$ from smoke is 40 percent, the effective biologic half-life is 25 days (*10*), and the intake of $^{210}Po$ is 0.036 pc per cigarette or 0.720 pc per pack [estimated from Kelley's data (*9*), which appear to best reflect acquisition by smokers], then a one-pack-per-day smoker accumulates at equilibrium only about 10 pc of total-body $^{210}Po$ from cigarettes—only a small fraction of the 600 pc (approximately) in an average man (*11*); even 100-percent retention of the $^{210}Po$ in the smoke from the daily smoking of one pack of cigarettes would lead to a maximum body content of 140 pc.

Table 2. Concentrations of $^{210}Pb$ in alveolar lung tissue of cigarette smokers and nonsmokers.

| Subject | | $^{210}Pb$ (pc/kg) |
|---|---|---|
| Age | Sex | |
| *Nonsmokers* | | |
| 53 | F | 2.4 |
| 49 | M | 0.6 |
| *Smokers* | | |
| 50 | M | 10.0 |
| 64 | M | 4.3 |
| 53 | F | 4.3 |
| 56 | M | 5.7 |

On the other hand, measurements on five sets of cigarettes smoked by the method of Kelley, 2 cigarettes per sample, show (Table 3) that the $^{210}Pb$ activity averages about two-thirds that of the $^{210}Po$ in the smoke. (Differences between the amounts of $^{210}Po$ found by us and by others probably reflect small differences in procedure; a more complete report is in preparation.) Thus, if we use two-thirds of Kelley's $^{210}Po$ activity as a minimum for $^{210}Pb$ activity [his values appear to be somewhat lower than most others (*1, 2, 4*)], with an estimated biologically effective half-life of 1600 days (*12*) for $^{210}Pb$, and conditions of intake similar to those of $^{210}Po$, a one-pack-per-day smoker (at equilibrium) accumulates 430 pc (estimated) of $^{210}Pb$ more than does a nonsmoker. This argument is analogous to an earlier statement (*11*) that, although concentration of $^{210}Po$ in tissue is important because it produces the actual dose, very little is acquired directly from food, water, and air—an amount about equal to our estimate from cigarettes. Its precursor, $^{210}Pb$, is usually the primary nuclide available to and stored by the body (*11*).

If the rib is considered to represent the skeleton, the radiation dose to the skeleton of a nonsmoker from the $^{210}Bi$-$^{210}Po$ series, in radioactive equilibrium with 0.135 pc of $^{210}Pb$ per gram of bone ash, is about 50 mrem/year—of a total skeletal dose rate of about 185 mrem/year. In this calculation it was assumed that the relative biologic effectiveness for alpha particles is 10, that the dose is homogeneously distributed, and that the doses contributed by the various sources are: $^{226}Ra$-$^{228}Ra$ series, 15 mrem/year; $^{40}K$ and $^{14}C$, 20 mrem/year; and external sources, 100 mrem/year (*13*). Thus, doubling the dose from the $^{210}Pb$-decay chain would increase the skeletal dose by as much as 30 percent; on the other hand, if the effective dose is that delivered to the 10-$\mu$ layer of surface cells of the bone, the increase in effective dose from smoke would be only about 8 percent.

Table 3. $^{210}Po$ and $^{210}Pb$ (per cigarette) in five samples of cigarette smoke. Average ratio ± S.D., .66 ± .23.

| $^{210}Po$ (pc) | $^{210}Pb$ (pc) | $^{210}Pb$ : $^{210}Po$ |
|---|---|---|
| 0.023 | 0.017 | .76 |
| .027 | .018 | .66 |
| .016 | .015 | .94 |
| .018 | .006 | .31 |
| .020 | .013 | .65 |

Our data demonstrate that, when one assesses the origins of these two nuclides in the human body, serious consideration should be given to the smoking habits of the populations concerned. This consideration is particularly important in epidemiological studies of low-level radiation, since the $^{210}Pb$ series contributes a substantial fraction of the skeletal dose resulting from internal emitters, if not of the total skeletal dose. Conversely, because of the tangible contribution of cigarette smoking to the skeletal dose, the incidence in smokers of diseases attributable to radiation (such as osteosarcoma and leukemia) deserves more than passing interest.

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**References and Notes**

1. E. P. Radford and V. R. Hunt, *Science* **143**, 247 (1964).
2. C. R. Hill, *Nature* **208**, 423 (1965).
3. B. Rajewsky and W. Stahlhofen, *ibid.* **209**, 1213 (1966).
4. E. S. Ferri and E. J. Baratta, *Public Health Rept. U.S.* **81**, 121 (1966).
5. C. Cogbill and M. E. Hobbs, *Tobacco* **144**(19), 24 (1951).
6. R. E. Nusbaum, E. M. Butt, T. C. Gilmour, S. L. DiDio, *Arch. Environ. Health* **10**, 227 (1965).
7. R. B. Holtzman, *Health Phys.* **9**, 385 (1963).
8. ———, *ibid.* **11**, 477 (1965).
9. T. F. Kelley, *Science* **149**, 537 (1965).
10. Intern. Comm. Radiol. Protection (1959); Committee II, *Health Phys.* **3**, 1 (1960).
11. R. B. Holtzman, *ibid.* **10**, 763 (1964).
12. ———, *ibid.* **8**, 315 (1962).
13. United Nations, *Report of the Scientific Committee on the Effects of Atomic Radiation: Suppl. 16 (A5216)* (1962), pp. 207, 414; R. E. Rowland, in *Argonne National Lab. Radiol. Phys. Div. Annual Rept. ANL-7060* (1965), p. 65.
14. Work performed under the auspices of the AEC. We thank William Lester for supplying the bone specimens and case histories.

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